General

Guideline Title

ACR Appropriateness Criteria® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women.

Bibliographic Source(s)

Moy L, Bailey L, D'Orsi C, Green ED, Holbrook AI, Lee SJ, Lourenco AP, Mainiero MB, Sepulveda KA, Slanetz PJ, Trikha S, Yepes MM, Newell MS, Expert Panel on Breast Imaging. ACR Appropriateness CriteriaÂ® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women. Reston (VA): American College of Radiology (ACR); 2016. 13 p. [68 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Moy L, Newell MS, Bailey L, Barke LD, Carkaci S, D'Orsi C, Goyal S, Haffty BG, Harvey JA, Hayes MK, Jokich PM, Lee SJ, Mainiero MB, Mankoff DA, Patel SB, Yepes MM, Mahoney MC, Expert Panel on Breast Imaging. ACR Appropriateness Criteria® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 12 p. [60 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Stage I Breast Cancer: Initial Workup and Surveillance for Local Recurrence and Distant Metastases in Asymptomatic Women

Variant 1: Newly diagnosed. Initial workup. Rule out bone metastases.

Radiologic Procedure	Rating	Comments	RRL*
FDG-PET/CT whole body	2		☢☢☢☢
Tc-99m bone scan whole body	1		☢☢☢
X-ray radiographic survey whole body	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	Radiation Level RRL*

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 2: Newly diagnosed. Initial workup. Rule out thoracic metastases.

Radiologic Procedure	Rating	Comments	RRL*
CT chest without IV contrast	2		☢☢☢
CT chest with IV contrast	2		☢☢☢
CT chest without and with IV contrast	2		☢☢☢
FDG-PET/CT whole body	2		☢☢☢☢
X-ray chest	1		☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 3: Newly diagnosed. Initial workup. Rule out liver metastases.

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen without IV contrast	2		☢☢☢
CT abdomen with IV contrast	2		☢☢☢
CT abdomen without and with IV contrast	2		☢☢☢☢
US abdomen	2		O
MRI abdomen without IV contrast	2		O
MRI abdomen without and with IV contrast	2		O
FDG-PET/CT whole body	2		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 4: Newly diagnosed. Initial workup. Rule out brain metastases.

Radiologic Procedure	Rating	Comments	RRL*
MRI head without IV contrast	2		O
MRI head without and with IV contrast	2		O
FDG-PET/CT whole body	2		☢☢☢☢
CT head without IV contrast	1		☢☢☢
CT head with IV contrast	1		☢☢☢
CT head without and with IV contrast	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 5: Surveillance. Rule out bone metastases.

Radiologic Procedure	Rating	Comments	RRL*
Tc-99m bone scan whole body	1		☢☢☢
X-ray radiographic survey whole body	1		☢☢☢
FDG-PET/CT whole body	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 6: Surveillance. Rule out thoracic metastases.

Radiologic Procedure	Rating	Comments	RRL*
X-ray chest	1		☢
CT chest without IV contrast	1		☢☢☢
CT chest with IV contrast	1		☢☢☢
CT chest without and with IV contrast	1		☢☢☢
FDG-PET/CT whole body	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 7: Surveillance. Rule out liver metastases.

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen without IV contrast	1		☢☢☢
CT abdomen with IV contrast	1		☢☢☢
CT abdomen without and with IV contrast	1		☢☢☢☢
US abdomen	1		O
MRI abdomen without IV contrast	1		O
MRI abdomen without and with IV contrast	1		O
FDG-PET/CT whole body	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 8: Surveillance. Rule out brain metastases.

Radiologic Procedure	Rating	Comments	RRL*
MRI head without IV contrast	1		O
MRI head without and with IV contrast	1		O
CT head without IV contrast	1		☢☢☢
CT head with IV contrast	1		☢☢☢
CT head without and with IV contrast	1		☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	RRL*
FDG-PET/CT wholebody	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Variant 9: Surveillance. Rule out local recurrence.

Radiologic Procedure	Rating	Comments	RRL*
Mammography diagnostic bilateral	9	Mammography may be designated as a diagnostic examination in patients with prior breast conserving therapy, even if asymptomatic. Frequency of imaging and duration of diagnostic surveillance may vary by institution, based on local protocol.	☢☢
Digital breast tomosynthesis diagnostic	9	Mammography may be designated as a diagnostic examination in patients with prior breast conserving therapy, even if asymptomatic. Frequency of imaging and duration of diagnostic surveillance may vary by institution, based on local protocol.	☢☢
Mammography screening	8	Patients with prior breast conserving therapy may be returned to routine screening at some point, dependent upon institutional protocol.	☢☢
Digital breast synthesis screening	8	Patients with prior breast conserving therapy may be returned to routine screening at some point, dependent upon institutional protocol.	☢☢
MRI breast without and with IV contrast bilateral	5	In selected patients, depending on risk assessment. May also be used as an adjunct tool in cases of scar versus recurrence. Should be performed in addition to, not as a replacement for, mammography.	O
US breast bilateral	5	As an adjunct screening alternative to MRI, in selected patients, if MRI is contraindicated. Should be performed in addition to, not as a replacement for, mammography.	O
MRI breast without IV contrast bilateral	1		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

The incidence of breast cancer has increased with more than 200,000 women diagnosed with invasive carcinoma yearly. Fortunately, breast cancer mortality has decreased due to advances in screening and improved treatment. As the proportion of women diagnosed with early-stage breast cancer increases, so too does the population of breast cancer survivors, emphasizing the importance of follow-up care for these women. The premise for intense monitoring in breast cancer survivors is that the detection of an early recurrence, prior to the development of symptoms, will allow for earlier treatment and can improve overall survival. However, randomized controlled trials have found that routine testing for distant metastatic disease provides no benefit in survival or health-related quality of life, and an intensive approach to surveillance is costly. Moreover, although many physicians and patients favor intensive initial workup and surveillance, patients overestimate the value of laboratory and imaging studies and may incorrectly perceive the significance of a normal test.

Initial Workup

This appropriateness guideline criteria segment addresses the initial imaging workup of women with stage I breast carcinoma, specifically regarding which imaging tests should be done to rule out unexpected metastatic disease.

Skeletal Metastases

Radionuclide scanning is more effective than conventional radiography for detecting skeletal metastases because radionuclide scans have higher sensitivity and can survey the entire skeleton in one examination. However, several investigations have revealed that bone scanning is not useful in stage I breast carcinoma because of its low yield and lack of proven effect on management or survival.

A large nonrandomized clinical study in Italy confirmed the lack of value of regular preoperative radiography and radionuclide bone scanning performed on stage I asymptomatic breast cancer patients. Only 1 of 633 patients with stage I disease had metastatic bone disease detected. Several other nonrandomized clinical studies have also documented the low yield and lack of utility of radionuclide bone scanning for patients with stage I breast carcinoma. Despite the low yield of bone scans, many clinicians order baseline bone scans for comparison with subsequent scans performed when patients develop symptoms or convert to an abnormal routine scan. In fact, routine baseline bone scans are unlikely to be useful in stage I disease because few patients will convert to positive scans. Also, earlier detection of metastases does not reduce overall mortality. Furthermore, several studies have reported false-positive scans when screening for metastases in asymptomatic patients.

The use of positron emission tomography (PET) combined with computed tomography (CT) in the initial staging of early-stage primary breast cancer is not well defined. It is uncertain whether PET/CT will serve as a replacement for current imaging technologies.

A retrospective study of 163 women with suspected metastatic breast cancer showed high concordance between PET/CT and bone scan in detecting bony metastases. Their results support the use of PET/CT in detecting osseous metastases and suggest that PET/CT may render bone scintigraphy unnecessary. Another study compared fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT and bone scintigraphy for detection of bone metastases in breast cancer in 132 lesions. The authors concluded that on a lesion basis whole-body PET/CT is more sensitive and equally specific for the detection of bone metastases compared with bone scintigraphy. Similarly, another study showed that PET/CT is significantly more accurate than bone scintigraphy for detecting bony metastases from breast and prostate cancers. Although PET/CT is more sensitive with similar specificity to scintigraphy, PET/CT is not routinely indicated for women with stage I breast cancer due to the very low incidence of metastatic disease.

Lung Metastases

Methods for detecting lung metastases include conventional chest radiography and CT. Because of its relatively low cost, conventional chest radiography is considered the most reasonable approach for detecting unsuspected disease, as a baseline for monitoring, and for routine follow-up. No information is available regarding whether PET/CT offers an advantage over current methods for detecting lung metastases.

Despite its relatively low cost, investigators have questioned the use of routine chest radiography in patients with breast cancer, especially those with stage I disease. One problem is its low yield, reported to be <0.5% in asymptomatic women who had routine chest radiographs after the diagnosis of stage I breast carcinoma. In a study of 412 women with newly diagnosed breast cancer, chest radiographs only showed metastasis in women previously classified as having stage III disease. Furthermore, false-positive chest radiographs can lead to expensive diagnostic workups. Two large Italian randomized control studies failed to show a significant outcome benefit when routine chest radiography was used to detect metastases earlier.

A recent retrospective study investigated the value of preoperative chest CT in detecting lung and liver metastases among 1,703 patients. Abnormal CT findings, in the lung or liver, were found in 266 patients (15.6%). Only 26 patients (1.5% of all patients and 9.8% of patients with abnormal CT findings) had true metastases. Only one patient with stage I disease had a true metastasis. They concluded that routine preoperative chest CT was not useful in detecting asymptomatic liver and lung metastasis in patients with early breast cancer.

Liver Metastases

It is rarely indicated to perform imaging to detect hepatic metastases in patients with stage I disease. Although liver metastases are not as common as lung or bone metastases, the appearance of liver metastases is associated with the worst prognosis. Ultrasound (US) can identify liver metastases ≥2 cm, and it is often used to localize these lesions for biopsy. No information is available regarding whether PET/CT offers an advantage over current methods for detecting liver metastases.

As with screening for bone and lung metastases, the yield of screening with radionuclide scans or US to detect asymptomatic liver metastases is low. A study showed the yield for detecting metastases using radionuclide scans or US to be <0.5%. A review of 4 studies evaluating a total of 423 women with stage I breast carcinoma found on liver US that no women had metastatic lesions. In a study of 412 women with newly diagnosed breast cancer, liver US only showed metastasis in women previously classified as having stage III disease. Large randomized control studies have failed to show a benefit from screening for liver metastases with US.

In the retrospective study described above, the sensitivity, specificity, and positive predictive value of CT were 100%, 97.6%, and 18.4%, respectively, for liver metastasis. Although CT and magnetic resonance imaging (MRI) may show more lesions than radionuclide scanning or US,

there is no evidence in the literature that routine imaging of the liver with either of the more sensitive modalities has clinical utility in asymptomatic patients with breast carcinoma.

Brain Metastases

Breast cancer is second only to lung carcinoma as a cause of intracerebral and orbital metastases, but few patients have brain metastases at the time of breast cancer diagnosis, particularly when the tumor is detected at stage I. One review of patients with breast cancer at all stages concluded that radionuclide brain scanning and CT failed to identify brain metastases in the absence of neurologic symptoms. A recent study prospectively explored the incidence of brain metastases during and after adjuvant trastuzumab administration in 258 patients with early-stage human epidermal growth factor receptor 2 positive (HER2+) breast carcinoma. They concluded that brain metastases are rare during adjuvant treatment and that brain CT screening is not justified in asymptomatic patients with early HER2+ breast carcinoma.

Because of its greater sensitivity, MRI has largely replaced CT for detecting and evaluating brain lesions. Gadolinium-enhanced MRI increases the number of suspected cerebral metastases that can be detected. Contrast-enhanced MRI has also been shown to be superior to double-dose delayed CT for detecting brain metastases. However, no studies suggest any usefulness to routine imaging with any modality for detecting cerebral metastases in asymptomatic women with breast cancer.

Surveillance

The most widely accepted guidelines regarding the surveillance of asymptomatic women with a history of breast cancer are from 2 national organizations: the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN). Both organizations state that routine surveillance with an annual mammogram is the only imaging test that should be performed to detect an in-breast recurrence or a new primary breast cancer. Several observational studies concluded that surveillance mammography detected locoregional recurrence and may reduce breast cancer mortality.

Local Recurrence

Local recurrence is defined as the return of cancer to the breast, lymph nodes, or chest wall after treatment. Most local recurrences occur within the first 5 years after diagnosis. The best predictor of local recurrence is whether the tumor margins contain cancer cells. The likelihood of local recurrence is lower when the tumor margins are negative. The risk of recurrence also depends on the status of the lymph nodes. Fortunately, most women are diagnosed with early-stage breast cancer, and the likelihood of local recurrence in 5 years for node-negative disease is 6.7%. If the lymph nodes are positive, the chance is 11%. The risk of local recurrence with lumpectomy plus radiation therapy can be lowered with chemotherapy and adjuvant hormonal therapy after surgery.

With mastectomy, the best predictor of local recurrence is how far the cancer has spread in the lymph nodes. The chance of local recurrence in 5 years is about 6% for women with negative lymph nodes. If 1 to 3 lymph nodes are positive, the chance of local recurrence in 5 years is about 16%. Radiation therapy can reduce this risk to about 2%.

Mammography is the imaging study used to follow women with a history of breast cancer. The role of breast MRI in screening women with a history of breast cancer is still being investigated. In 2007 the American Cancer Society published its guidelines for breast cancer screening with MRI as an adjunct to mammography. These guidelines state that in women with a personal history of breast cancer and no other risk factor, there is insufficient evidence to recommend for or against breast MRI. A group of researchers found a cancer yield of 12% (17/144) in women with a personal history of breast cancer using screening MRI. High-risk women with prior lumpectomy and a very strong family history may be considered for MRI screening. See the National Guideline Clearinghouse (NGC) summary American College of Radiology (ACR) Appropriateness Criteria® breast cancer screening.

Digital breast tomosynthesis (DBT) addresses some of the limitations encountered with standard mammographic views. In addition to planar images, DBT allows for creation and viewing of thin-section reconstructed images that may decrease the lesion-masking effect of overlapping normal tissue, and reveal the true nature of potential false-positive findings. DBT can be useful in the diagnostic setting, improving lesion characterization in noncalcified lesions, when compared to conventional mammographic workup. Interpretation time for DBT images is greater than for standard mammography. Additionally, dose is increased if standard two-dimensional (2-D) images are obtained in addition to DBT images. However, synthesized reconstructed images (a virtual planar image created from the tomographic data set) may replace the need for a 2-D correlative view; and current data suggests that these synthetic images perform as well as standard full-field digital images

Distant Recurrence (Metastasis)

Metastasis is the main cause of breast cancer death. The risk of distant recurrence is the same for women who undergo lumpectomy and radiation therapy or women who have a mastectomy. The most common sites for distant metastases from breast carcinoma are the skeleton, lung, liver, and brain. Surveys of patients with breast cancer indicate that most of them prefer an intensive follow-up to detect asymptomatic disease, including

metastases. Surveys of physicians indicate that most of them also favor intensive surveillance programs in asymptomatic patients. However, because of cost constraints there should be a reasonable expected effect on patient management and outcome when imaging examinations are ordered on asymptomatic patients. In a review by the Cochrane Collaboration of 4 randomized, controlled clinical trials that included 3,055 women, a group of authors found no difference in overall or disease-free survival rates for women who underwent intensive radiologic and laboratory testing compared with those managed with clinical visits and mammography. They concluded that a regular physical and yearly mammogram is as effective as more intense methods of examination in detecting recurrent breast cancer.

Two multicenter randomized prospective clinical trials were performed in Italy in the 1980s in asymptomatic breast cancer survivors. One study randomized 1,320 women into a study group that would undergo "intensive surveillance" and a control group having only tests that were ordered as a result of subsequent clinical findings uncovered at routine medical visits. The intensive surveillance included radionuclide bone scanning, chest radiography, and liver US. The study, which included 739 node-negative women, found that metastases of all kinds were detected only an average of 1 month earlier in the intensive surveillance group. The earlier detection of these metastases had no significant effect on overall survival.

A second large clinical trial in Italy randomized 1,243 women into "intensive" and "clinical" follow-up protocols to determine whether early detection of bone and intrathoracic metastases was effective in reducing mortality in the intensive follow-up group. Fifty-two percent of the women in the latter study were node-negative. Although more bone and lung metastases were found in the intensive follow-up group, there was no significant difference in the overall 5-year survival rates between the 2 groups.

As discussed above, national guidelines advise against routine surveillance testing (at regular predefined intervals), including routine blood tests, blood tests for tumor markers, chest radiographs, bone scans, liver US, abdominal CT scans, and PET/CT scans. However, clinical practices often do not adhere to these guidelines. Using the Surveillance, Epidemiology, and End Results (SEER) Medicare data, a group of researchers studied 44,591 women who were diagnosed with stage I/II breast cancer from 1992 to 1999 and followed through 2001. They found that women receiving care from medical oncologists had substantially higher rates of testing with more bone scans, tumor antigen tests, chest radiographs, and other chest/abdominal imaging than women followed by their primary health provider. Overall, the rates of testing decreased over time. Rates of tumor antigen testing and chest radiographs decreased faster than chest/abdominal imaging.

One study recently evaluated the use of high technology radiologic imaging (HTRI) for surveillance after curative treatment for early-stage breast cancer. Using the SEER-Medicare data, they identified 25,555 women who were diagnosed with stage I/II breast cancer between 1998 and 2003 who survived more than 48 months. Over time, the use of CT, bone scans, breast MRI, and PET increased from 34% of women diagnosed in 1998 to 43% in women diagnosed in 2003. Forty percent of their cohort had at least one advanced imaging examination, and 30% had CT scans. Factors associated with HTRI use were women age <80, higher comorbidity index, stage II disease, and more recent diagnosis. Another group of researchers found similar results when they reviewed the preoperative use of advanced imaging modalities in early-stage breast cancer. Using the SEER Medicare data from 1992 to 2005, the authors identified 67,874 stage I/II breast cancer patients. Approximately 19% (n=12,740) had preoperative advanced imaging. The proportion of patients having CT scans, PET scans, and brain MRI scans increased from 5.7% to 12.4% (P<.0001), 0.8% to 3.4% (P<.0001), and 0.2% to 1.1% (P=.008), respectively, from 1992 to 2005. Bone scans declined from 20.1% to 10.7% (P<.0001). They concluded that greater adherence to current guidelines is warranted.

Refer to the original guideline document for results from other studies and a discussion of quality-of-life issues.

Summary of Recommendations

- Given the lack of difference in survival or quality of life, there is little justification for imaging to detect or rule out metastasis in asymptomatic women with newly diagnosed stage I breast cancer.
- Women and health care professionals generally prefer intensive follow-up after a diagnosis of breast cancer. Women with other risk factors that increase their lifetime risk for breast cancer may warrant evaluation with breast MRI. However, quality of life is similar for women who undergo intensive surveillance compared with those who do not.
- ASCO and NCCN guidelines state that annual mammography is the only imaging examination that should be performed to detect a localized breast recurrence in asymptomatic patients; more imaging may be needed if the patient has locoregional symptoms (e.g., palpable abnormality).
- There are no survival differences between women who obtain intensive screening and surveillance with imaging and laboratory studies compared with women who only undergo testing due to the development of symptoms or findings on clinical examinations.

Abbreviations

- CT, computed tomography
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
- IV, intravenous

- MRI, magnetic resonance imaging
- Tc-99m, technetium-99 metastable
- US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Stage I breast cancer

Guideline Category

Evaluation

Screening

Clinical Specialty

Internal Medicine

Nuclear Medicine

Obstetrics and Gynecology

Oncology

Radiology

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging procedures for initial workup and surveillance for local recurrence and distant metastases in asymptomatic women with stage I breast cancer

Target Population

Asymptomatic women with stage I breast cancer

Interventions and Practices Considered

1. X-ray
    - Radiographic survey, whole body
    - Chest
2. Technetium (Tc)-99m bone scan, whole body
3. Computed tomography (CT)
    - Chest without and with intravenous (IV) contrast
    - Chest with IV contrast
    - Chest without IV contrast
    - Abdomen without and with IV contrast
    - Abdomen with IV contrast
    - Abdomen without IV contrast
    - Head without and with IV contrast
    - Head with IV contrast
    - Head without IV contrast
4. Magnetic resonance imaging (MRI)
    - Abdomen without and with IV contrast
    - Abdomen without IV contrast
    - Head without and with IV contrast
    - Head without IV contrast
    - Breast without IV contrast, bilateral
    - Breast without and with IV contrast, bilateral
5. Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET)/CT, whole body
6. Ultrasonography (US)
    - Abdomen
    - Breast, bilateral
7. Mammography
    - Diagnostic bilateral
    - Screening
8. Digital breast tomosynthesis
    - Diagnostic
    - Screening

Major Outcomes Considered

- Utility of radiologic examinations in staging and detection of recurrence and metastases
- Quality of life
- Risk of recurrence
- Overall, disease-free, and 5-year survival rate
- Rates of testing
- Accuracy, sensitivity, and specificity of radiologic examinations
- False-positive and false-negative rates

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 60 citations in the original bibliography, 59 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in July 2015 to identify additional evidence published since the *ACR Appropriateness Criteria® Stage 1 Breast Cancer* topic was finalized. Using the search strategies described in the literature search companion (see the "Availability of Companion Documents" field), 161 articles were found. Nine articles were added to the bibliography. One hundred fifty-two articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased, or the articles were already cited in the original bibliography.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of Companion Documents" field) for further information.

Number of Source Documents

Of the 60 citations in the original bibliography, 59 were retained in the final document. The new literature search conducted in July 2015 identified nine articles that were added to the bibliography.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

> The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
>
> *Or*
>
> The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
>
> *Or*
>
> The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness. When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4,

5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the second rating round, the recommendation is "May be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Imaging tests to detect an occult metastasis in a breast cancer survivor may be beneficial, for example, by allowing patients to avoid unnecessary surgery or potentially allowing for less aggressive treatment that could impact quality of life. However, the lack of adherence to guidelines for imaging tests to detect recurrent breast cancer is associated with higher medical costs and additional radiation risks. Studies estimate that intensive surveillance testing adds an additional $260 million to $630 million to the annual cost of breast cancer survivors without demonstrated benefit compared with a strategy that follows national guidelines.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of the Evidence

Of the 68 references cited in the *ACR Appropriateness Criteria® Stage I Breast Cancer: Initial Workup and Surveillance for Local Recurrence and Distant Metastases in Asymptomatic Women* document, 63 references are categorized as diagnostic references including 3 well designed studies, 6 good quality studies, and 15 quality studies that may have design limitations. There are 42 references that may not be useful as primary evidence. There are 2 references that are meta-analysis studies.

While there are references that report on studies with design limitations, 9 well designed or good quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

The premise for intense monitoring in breast cancer survivors is that the detection of an early recurrence, prior to the development of symptoms, will allow for earlier treatment and can improve overall survival. However, randomized controlled trials have found that routine testing for distant metastatic disease provides no benefit in survival or health-related quality of life, and an intensive approach to surveillance is costly. Moreover, although many physicians and patients favor intensive initial workup and surveillance, patients overestimate the value of laboratory and imaging studies and may incorrectly perceive the significance of a normal test.

Potential Harms

- Several studies have reported false-positive scans when screening for metastases in asymptomatic patients.
- False-positive chest radiographs can lead to expensive diagnostic workups.
- Occasionally, additional imaging studies will generate false-positive examinations. These findings may lead to follow-up imaging studies, biopsies, and possibly surgery. One study concluded that clinicians have sold their patients on the promise of advanced imaging and neglected to educate them about the detrimental effects of excess exposure to radiation, additional testing brought about by chasing false-positive results, or the anxiety related to these studies. Ordering advanced imaging studies may provide patients with short-term reassurance but seldom allays long-term fears of recurrence that are ubiquitous in cancer survivors.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the American College of Radiology (ACR) Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.
- ACR seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Moy L, Bailey L, D'Orsi C, Green ED, Holbrook AI, Lee SJ, Lourenco AP, Mainiero MB, Sepulveda KA, Slanetz PJ, Trikha S, Yepes MM, Newell MS, Expert Panel on Breast Imaging. ACR Appropriateness CriteriaÂ® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women. Reston (VA): American College of Radiology (ACR); 2016. 13 p. [68 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Breast Imaging

Composition of Group That Authored the Guideline

Panel Members: Linda Moy, MD (*Principal Author*); Lisa Bailey, MD; Carl D'Orsi, MD; Edward D. Green, MD; Anna I. Holbrook, MD; Su-Ju Lee, MD; Ana P. Lourenco, MD; Martha B. Mainiero, MD; Karla A. Sepulveda, MD; Priscilla J. Slanetz, MD, MPH; Sunita Trikha, MD; Monica M. Yepes, MD; Mary S. Newell, MD (*Panel Chair*)

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Moy L, Newell MS, Bailey L, Barke LD, Carkaci S, D'Orsi C, Goyal S, Haffty BG, Harvey JA, Hayes MK, Jokich PM, Lee SJ, Mainiero MB, Mankoff DA, Patel SB, Yepes MM, Mahoney MC, Expert Panel on Breast Imaging. ACR Appropriateness Criteria® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women [online publication]. Reston (VA): American College of Radiology (ACR); 2014. 12 p. [60 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2015 Sep. 3 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2016. 128 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2016 May. 2 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women. Evidence table. Reston (VA): American College of Radiology; 2016. 24 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® stage I breast cancer: initial workup and surveillance for local recurrence and distant metastases in asymptomatic women. Literature search. Reston (VA): American College of Radiology; 2016. 1 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on January 30, 2001. The information was verified by the guideline developer as of February 20, 2001. This summary was updated by ECRI on March 31, 2003. The updated information was verified by the guideline developer on April 21, 2003. This NGC summary was updated by ECRI Institute on May 17, 2007. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on May 12, 2010. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on February 7, 2012, July 16, 2014, and September 14, 2016.

Copyright Statement

Disclaimer

NGC Disclaimer